REMARKS

Applicants are grateful for the entry of the amendments submitted in Applicants' response dated May 19, 2005.

This amendment is responsive to the Final Office Action mailed August 5, 2005 and to the teleconference held with the Examiner October 26, 2005. In the instant Office Action, claims 1-3, 5-24 and 26 are listed as pending, and claims 1-3, 5-24 and 26 are listed as rejected. Applicants have amended claims 1, 5, 7, 8 and 16-24 and have filed new claims 27 and 28. Claims 4 and 25 remain cancelled; claims 2, 3, 9-15 and 26 are now cancelled with this reply.

Text in the specification in support of the amendments is as follows:

In the specification, text at page 4, lines 5-22, text at page 17 lines 3-9 and Figure 7, text beginning on page 17 line 30 and continuing to page 18 line 21 and Figures 10 and 11, and originally filed claim 8 support amending claim 1 to recite treatment of breast cancer and characterizing the levels of PBR in a cancer prior to treatment with a Ginkgo biloba extract containing Ginkgolide B or with Ginkgolide B alone. Text at page 1 lines 9-15, text at page 8, lines 4-26, text beginning on page 9 line 16 and continuing to page 10 line 6, text beginning on page 16 line 26 and continuing to page 17 line 2, and Figures 4, 5, 6, 10 and 11 support the amendment to claim 1 that the method of treatment inhibits the proliferation of breast cancer cells.

Dependent claim 5 is amended to conform to amendments to claim 1.

In the specification, text at page 12 lines 18-26 and page 16, lines 12-19 as well as Figures 1 and 2 support amending claims 7 and 8 to recite breast cancer cells (claim 7) and in particular, human breast cancer cells (claim 8). The amendments also conform dependent claims 7 and 8 to newly amended claim 1.

Dependent claim 16 is amended to conform to amendments to claim 1.

In the specification, text at page 17 lines 18-29, beginning on page 19 line 3 and continuing to page 20 line 3, Figure 9 and Table 1 support the amendments to claims 17-24 such

that the administering of a Ginkgo biloba extract containing Ginkgolide B affects gene expression.

In the specification, text at page 7 lines 10-13 supports new claims 27-28.

Applicants reserve the right to reclaim the cancelled subject matter in a subsequent application.

REMARKS REGARDING THE TELECONFERENCE

Applicants are also grateful for the October 26, 2005 teleconference which the Examiner granted to Applicants' representatives, Attorney Brian Morrill and the undersigned. As agreed, Applicants provide herewith a summary of the topics discussed in the teleconference.

The teleconference began with Applicants' representatives initially suggesting further amendments to independent method claim 1. Claim 1 was previously amended in the May 19, 2005 response to the first Office Action to limit the method to treatment of a cancer characterized by an over-expression of peripheral-type benzodiazepine receptor protein (PBR). Applicants' representatives proposed to further modify the claim to include a screening step. The screening step instructs the practitioner to determine the level of PBR in the cancerous tissue prior to treatment with a Ginkgo biloba extract containing GKB or with isolated GKB.

Summarized herewith are the various allegations and general comments set forth by the Examiner and Applicants' Representatives during the teleconference.

First, the Examiner alleged that the addition of a new step to the method would require a new search. During the teleconference, the Examiner repeatedly alleged that the references cited against the application (DE 42 08 868, EP 0 359 951 and U.S. 6,316,690 to Fogarty, referred to hereinafter as DE '868, EP '951 and Fogarty, respectively) taught the treatment of cancer with Ginkgo biloba. The Examiner opined that Applicants' limitation to cancer characterized by increased levels of PBR was irrelevant as the art disclosed Ginkgo biloba and cancer.

Second, the Examiner alleged that a person in a laboratory would not know if a cancer exhibited increased levels of PBR. The Examiner further alleged that Applicants did not show that cancer cells with increased levels of PBR react differently to a Ginkgo biloba extract than cancer cells that did not have increased levels of PBR. The Examiner indicated that had Applicant demonstrated such, this would have been inventive over the art.

Third, after being directed to *in vitro* data in the specification which demonstrated that cells having increased levels of PBR do indeed react differently to a Ginkgo biloba extract than do cancer cells not having increased levels of PBR, the Examiner queried as to the availability of *in vivo* data.

Fourth, the Examiner alleged that the DE '868 and EP '951 references taught the "synergy" of Ginkgo biloba and other cancer drugs to effect improved cancer treatment. The Examiner opined that synergy exists when individual components that have their own activity work together for better activity and thus, the Ginkgo biloba alone must have had some anti-cancer activity. Interestingly, the Examiner later opined that "extracts don't work", could not be well characterized, and further alleged that components within a given extract may act against each other.

The Examiner reiterated several times during the teleconference that neither the mechanism of cancer progression nor the level of PBR were relevant to Applicants' invention because the prior art references disclosed cancer treated with Gingko biloba.

In response to the Examiner's allegations, Applicants' representatives responded with the following comments and questions.

With respect to the first allegation, Applicants' representatives respectfully queried as to the nature of the searches carried out against the claimed invention. The Examiner noted that his search was limited to Ginkgo biloba and cancer, as recited in Applicants' originally filed claim 1. Importantly, the Examiner conceded that, in fact, no search was carried out with respect to the subject matter of previously amended claim 1 (see Applicants' May 19, 2005 reply) which recited treatment of a cancer characterized by increased levels of PBR, and further that no search was carried out with respect to the various oncogenes or types of cancers recited

in the various dependent claims. The Examiner indicated that because he had identified references which allegedly disclosed treatment of cancer with Ginkgo biloba, it was not necessary to search Applicants' added limitation requiring that the cancer to be treated exhibit increased levels of PBR. The Examiner was unable, however, to identify a single instance in which references EP '951, DE '868 or Fogarty discussed the PBR receptor at all, much less the levels of PBR receptor expression, much less still that levels of PBR in a cancer cell could be used to select which cancer would be particularly responsive to treatment with a Ginkgo biloba extract containing Ginkgolide B or with isolated Ginkgolide B.

With respect to the second allegation, Applicants' representatives directed the Examiner to the instant specification which clearly sets forth a number of methods to screen a tissue for the presence or absence of PBR protein and/or RNA, thus enabling a practitioner to determine if a cancer exhibited increased levels of PBR (see for example, the specification at page 13 line 21 through page 14 line; page 14 lines 4-17; page 14 lines 18-33; page 15 lines 1-8; and page 15 lines 9-15, all of which were identified in Applicants' response of May 19, 2005). Applicants' representatives further pointed out that data presented in the instant specification clearly demonstrate that a breast cancer cell line characterized by high levels of PBR expression (the MDA-231 cell line) was affected by application of a Gingko biloba extract to a much greater extent than was a breast cancer cell line characterized by low levels of PBR expression (the MCF7 cell line; see page 17, lines 3-9 and Figure 7).

With respect to the third allegation, Applicants' representatives respectfully directed the Examiner to the portion of the instant specification describing the ability of Ginkgo biloba extract to retard the growth of human breast cancer cells expressing high levels of PBR grafted into a mouse host (see for example, page 17, line 30 through page 18, line 21, and to Figures 10 and 11, all of which were identified in Applicants' response of May 19, 2005).

With respect to the fourth allegation, Applicants' representatives respectfully pointed out that references EP '951 and DE '868 could not teach synergy of Ginkgo biloba and other cancer treatments as neither reference provided any evidence as to the effect of a Ginkgo biloba extract alone upon cancer. Applicants' representatives pointed out that the references only

taught that Ginkgo biloba may act as a free radical scavenger or to ameliorate side effects of particular cancer drugs (see EP '951 specification at column 2 paragraph 2; also DE '868 specification at page 4, column 1 paragraphs 7-9). Applicants' representatives pointed out that the references failed to teach that administration of Gingko alone is efficacious in treating cancer and, as such, the prior art references could not possibly teach or suggest that abnormally high levels of PBR in a cancer would render that cancer more susceptible to treatment with Ginkgo biloba.

In conclusion, as the application is under Final Rejection, the Examiner encouraged Applicants to file a continuing application rather than allowing additional amendments to the claims. The Examiner suggested further limiting amended claim 1 to the use of Ginkgolide B or a treatment consisting essentially of Ginkgolide B rather than a Ginkgo biloba extract. The Examiner was of the opinion that "extracts don't work" since they are varied and complicated mixtures in which components potentially act against one another. In response to the Examiner's comment that plant extracts are unreliable, Applicants remind the Examiner that the claims of the instant application are not drawn to all plant extracts, but rather to an extract of Ginkgo biloba. Applicants' representatives suggested further amending the claims to read upon breast cancer, which seemed acceptable to the Examiner. In response to the Examiner's suggestions, submitted herewith are amended claims and a Request for Continued Examination in compliance with 37 C.F.R. §1.114.

Applicants also submit herewith an Information Disclosure Statement. The IDS recites excerpts from two DeFeudis references (cited in the specification at page 1, lines 26-30 and page 2 lines 6-7) showing that extracts from the Ginkgo biloba tree, particularly Gingko biloba extract EGb 761®, are well characterized, standardized plant extracts. The IDS also recites two recently published abstracts in which the authors demonstrated that application of Ginkgo biloba to ovarian cell cancer line OVCA433 inhibited cell growth by about 70% to 80% and concluded from a population-based study that "Ginkgo biloba, and specifically its ginkgolide components, may have value in the prevention of ovarian cancer" (Ye *et al.*, "Epidemiological and biological evidence for protective effect of ginkgo biloba on ovarian cancer," 2005, 96th

Annual Meeting of the American Association for Cancer Research, April 16-29, Anaheim/Orange County, CA, Abstract #3484; Ye *et al.*, "Ginkgo biloba and ginkgolides as potential agents for ovarian cancer prevention," 2005, Frontiers in Cancer Prevention Research Meeting, October 30-November 2, Baltimore, MD, Abstract #A100.). The IDS further recites a recently published press release ("Gingko may prevent ovarian cancer," Brigham and Women's Hospital Press Release, October 31, 2005) in which investigators Ye and Cramer (of Ye *et al., supra*) report that of the Ginkgo, Echinacea, St. John's Wort, and Ginseng herbal extracts used by the participants of the biological study, only the Ginkgo extract was found to be linked to ovarian cancer prevention. Applicants respectfully submit that these references demonstrate that, contrary to the Examiner's position that "plant extracts don't work," plant extracts do indeed "work" and that Ginkgo is an especially useful plant extract.

REMARKS REGARDING CLAIM REJECTIONS IN THE FINAL OFFICE ACTION

1. Claim Rejections – 35 U.S.C. § 112, First Paragraph

A) Rejection of claims 1-3, 5-24 and 26 *under 35 U.S.C. § 112, first paragraph*

On pages 2-3 of the instant Office action, the Examiner rejects claims 1-3, 5-24 and 26 under 35 U.S.C. § 112, first paragraph, for lack of enablement. More specifically, on page 2 of the instant Office Action the Examiner alleges that the specification,

> "while being enabling for *in vitro* inhibition of MDA-231 cells by Ginkgolide B, does not reasonably provide enablement for the generic 'a method of combating cancer by Ginkgolide B or Ginkgo biloba extracts'."

Beginning on page 2 and continuing to page 3 of the instant Office Action, the Examiner further alleges that:

> "Just because a specific component is effective in the expression of a specific gene or effective in *in vitro* inhibition of a specific cancer cell cultures, one cannot draw a conclusion that either an extract containing that specific compound or the specific compound itself is effective in the *in vivo* treatment of various cancers. Instant specification lacks adequate description to come to that conclusion."

The Examiner goes on to conclude that:

> "Broad claims must have broad basis for support in the specification. In the absence of such support, claims must be limited to the *in vitro* effectiveness of Ginkgolide B in inhibiting MDA-231 cells in culture."

The Examiner did not find Applicants' arguments of May 19, 2005 persuasive because

> "many components are affected in cancer cells, which may or may not be causative factors for the cells to become cancerous. Just because this compound reduces the breast tumor sizes of implanted breast cancer cells which express high amounts of these receptors does not necessarily mean that it is effective against all cancers since applicants have not established benzodiazepine receptors are causative factors." (emphasis added)

B) 35 U.S.C. § 112, first paragraph

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 112 appearing on page 2 of the instant Office Action that forms the basis for the rejection under this section:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

C) Amended and cancelled claims

Applicants note that claims 1, 5, 7, 8, and 16-24 have been amended in the instant specification, and claims 27-28 are new. Claims 2, 3, 9-15, and 26 have been cancelled from the instant application, thus the rejection thereof under 35 U.S.C. § 112, first paragraph, has been obviated for these claims.

D) Claims 1-3, 5-24 and 26 are fully enabled as required by 35 U.S.C. § 112

Applicants respectfully reiterate in full the arguments made in Applicants' May 19, 2005 reply. Applicants respectfully submit that in the instant Office Action, and as evidenced by comments made by the Examiner during the October 26, 2005 teleconference, the Examiner

continues to misinterpret the claimed method as being a "one cancer agent" applicable to "all cancers" when Applicants have clearly specified a narrow, identifiable class of cancers, namely those over-expressing PBR. Applicants also submit that the Examiner has not demonstrated how the instant application fails to enable the skilled artisan to determine whether a cancer cell is characterized by high levels of PBR or to use isolated GKB or a Ginkgo extract containing GKB to treat such cancer. To the contrary, Applicants provide ample teachings from the literature (see specification beginning on page 2 line 14 and continuing to page 3 line 2) as well as experimental teachings (see specification beginning at page 13 line 21 and continuing to page 15, line 15; page 17 line 30 to page 18 line 21) to guide the skilled artisan to determine whether a cancer is characterized by an over-expression of PBR.

Applicants submit that the Examiner has also failed to appreciate that the claimed method allows the skilled person to select cancers which may be more amenable to treatment with an effective amount of isolated GKB or a Ginkgo extract containing GKB. The Examiner acknowledges that "this compound reduces the breast tumor sizes of implanted breast cancer cells which express high amounts of these receptors" yet the Examiner alleges that this finding "does not necessarily mean that it is effective against all cancers since applicants have not established benzodiazepine receptors are causative factors." Applicants make no claim as to the causative agent of the cancer; Applicants' method is not intended to induce cancer but rather to treat it. Applicants submit that the Examiner has not presented any legal or scientific reason why the benzodiazepine receptors characterizing cancer cells are required to be a causative agent in order for the Gingko biloba extract or isolated GKB to be an effective treatment.

Regardless of the causative factors in a given cancer, Applicants demonstrate that elevated levels of PBR receptor are a reliable indicator that treatment with a Ginkgo biloba extract containing GKB or with isolated GKB would be particularly effective. Applicants have clearly demonstrated to the skilled artisan how to determine whether a cancer exhibits high levels of PBR by either A) relying upon the body of knowledge in the literature available at the time of filing (see specification beginning on page 2 line 14 and continuing to page 3 line 2) or

B) carrying out laboratory determinations to characterize the levels of PBR in a given cancer (see specification beginning at page 13 line 21 and continuing to page 15, line 15; page 17 line 30 to page 18 line 21). Applicants submit that these teachings, as well as Applicants *in vitro* and *in vivo* data presented in the instant specification referenced above, clearly demonstrate to the skilled artisan that application of a Ginkgo biloba extract containing GKB or isolated GKB would be particularly effective treatment for cancers exhibiting high levels of PBR.

Applicants also respectfully submit that the Examiner has failed to acknowledge Applicants' *in vivo* and *in vitro* teaching as being enabling while at the same time the Examiner acknowledges as enabling disclosure with far less support. On page 2 of the instant Office Action, the Examiner states that "just because a specific component is effective in the expression of a specific gene or effective in *in vitro* inhibition of a specific cancer cell cultures, one cannot draw a conclusion that either an extract containing that specific compound or the specific compound itself is effective in the *in vivo* treatment of various cancers." On page 3 of the instant Office Action, the Examiner alleges that "it is a well known fact that one cancer agent cannot effectively treat all types of cancers." However, later in the Office Action the Examiner relies upon Fogarty which discloses a list of plant or herbal extracts which allegedly function in a *Drosophila* model system to reduce transgenically-induced tumors, as fully supporting the use of the undefined plant and herbal extracts for treating hepatic, colon, leukemia, lymphoma, glioma, breast, prostate, pancreas, bladder, melanoma and lung cancers (page 6 of the Instant Action). In the teleconference, the Examiner repeatedly relied upon the DE '868 and EP '951 references as teaching that a Ginkgo biloba extract alone or Ginkgolide B alone may be used to treat all cancers. Applicants respectfully submit that these two references disclose only that Ginkgo biloba may be a useful adjunct in the treatment of certain cancers, i.e., that co-administration of a Ginkgo product with traditional cancer chemotherapy agents may, in some unknown manner, allow "a reduction of undesired effects of the chemotherapy" (EP '951, column 2, paragraph 2) or perhaps "allow a renewed response to the cytotoxic agent" (see DE '868, page 4, column 1, paragraph 8).

Applicants respectfully question how the Examiner can view Fogarty's data from *Drosophila* and the statements in the DE '868 and EP '951 references (which lack actual data) as supportive for so many types of cancers when, at the same time, the Examiner fails to find enabling Applicants *in vitro* and *in vivo* data in mouse showing that human breast cancer cells specifically characterized by an over-expression of PBR respond to application of Ginkgo biloba extract or GKB differently as compared to breast cancer cells which are not characterized by an over-expression of PBR.

Without conceding to the correctness of the Examiner's objections and allegations expressed both in the instant Office Action and in the October 26, 2005 teleconference, Applicants have further limited the method of claim 1 and as such, subsequent dependent claims, to the of treatment of breast cancer over-expressing PBR in which the practitioner firstly determines whether the level of PBR expression in breast cancer cells is elevated relative to a normal cell. Applicants teach that if the level of PBR is elevated in the breast cancer cells at least 3-fold as compared to normal cells, the practitioner should consider the use of isolated GKB or of a Ginkgo extract containing GKB to treat such breast cancer.

E) Request for withdrawal of rejection of claims 1-3, 5-24 and 26 under 35 U.S.C. § 112, first paragraph

Applicants submit that, for reasons cited above and amendments presented herein, the specification fulfills the enablement requirement of 35 U.S.C. § 112, first paragraph and respectfully request that the rejection of claims 1, 5-8, 16-24 and new claims 27-28 under 35 U.S.C. § 112, first paragraph, has been obviated. Applicants respectfully request that said rejection be withdrawn.

2. Claim Rejections – 35 U.S.C. § 102(b)

A) Rejection of claims 1-3, 5-7, 16-24 and 26 under 35 U.S.C. § 102(b)

On pages 3-5 of the instant Office action, the Examiner rejects claims 1-3, 5-7, 16-24 and 26 under 35 U.S.C. § 102(b) as being anticipated by DE '868 or EP '951.

On page 4 of the instant Office Action, the Examiner alleges that DE '868 and EP '951 each disclose a method of treatment of cancer using a Ginkgo biloba extract, a position he maintained in the October 26, 2005 teleconference. The Examiner also alleges on page 4 that "the mechanism by which the composition of the prior art functions has no patentable significance since it is the inherent effect of the prior art extract."

The Examiner alleges that the Applicants arguments are not persuasive because (pages 4-5 of the Instant Action):

> "instant claim language 'comprising' does not exclude the other anti-cancer agents in the references. Furthermore, it would appear that the references teach synergism of the extract and the other anti-cancer agents and this implies that each agent has some activity by itself and when combined, they show an enhanced activity. This is evident from claim 1 in EP '951 and DE '868 where only the extract for the treatment of metastatic cancer is recited. Applicant's arguments with regard to both references fail to teach that over expression of PBR is a distinguishable and testable attribute of cancer cells that may be used to determine which patients may be most amenable to treatment with Ginkgo extract containing GKB or with isolated GKB, the examiner points out that instant claims are drawn to 'a method of combating cancer which is characterized by an over-expression of peripheral-type benzodiazepine receptor protein (PBR protein)' and not to 'a method of interaction of Ginkgo extract containing GKB or isolated GKB with peripheral-type benzodiazepine receptor protein' and applicant has not shown that the cancer taught by the prior art does not have peripheral-type benzodiazepine receptor protein. As already pointed out, the mechanism by which GKB or extract containing GKB acts to have an effect on cancer cells has no significance."

B) 35 U.S.C. § 102(b)

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 102(b) that forms the basis for the rejection under this section, as pointed out by the Examiner on page 3:

> A person shall be entitled to a patent unless -
>
> 35 U.S.C. § 102(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the applicant for patent in the United States, or

C) Amended and cancelled claims

Applicants note that claims 1, 5, 7, 8, and 16-24 have been amended in the instant specification, and claims 27-28 are new. Claims 2, 3, 9-15 and 26 have been cancelled from the instant application, thus the rejection thereof under 35 U.S.C. § 112, first paragraph, has been obviated for these claims.

D) Claims 1-3, 5-7, 16-24 and 26 are not anticipated by DE 42 08 868 or EP 0 359 951 under 35 U.S.C. § 102(b)

Applicants respectfully reiterate in full the arguments made in Applicants' May 19, 2005 reply. Applicants also respectfully submit that the present amendments to the method of claim 1, and therefore of dependent claims 5-8, 16-24, 27 and 28, even further distinguish Applicants' method from the teachings of references DE '868 and EP '951. Applicants submit that neither reference teaches nor suggests to the practitioner to determine whether the levels of PBR in breast cancer cells are elevated and, upon finding elevated levels of PBR (*i.e.*, at least 3-fold greater than a normal cell), to administer an effective amount of a Ginkgo biloba extract containing GKB or of isolated GKB to treat the breast cancer.

E) Request for withdrawal of rejection of claims 1-3, 5-7, 16-24 and 26 under 35 U.S.C. § 102(b)

Applicants submit that, for reasons cited above and amendments presented herein, the rejection of newly amended claims 1, 5, 7, 16-24, original claim 6, and new claims 27-28 under 35 U.S.C. § 102(b) over DE '868 and EP '951 has been obviated. Applicants request that said rejection be withdrawn.

3. Claim Rejections – 35 U.S.C. § 102 (e)

A) Rejection of claims 1-3, 5-9, 12, 13, 15-24 and 26 under 35 U.S.C. § 102(e)

On pages 5-6 of the instant Office action, the Examiner rejects claims 1-3, 5-9, 12, 13, 15-24 and 26 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent 6,316,690 to Fogarty (referred to hereinafter as "Fogarty").

The Examiner maintains that Fogarty discloses the anti-tumor activity of a Ginkgo biloba extract against a variety of tumors, including hepatic, colon, leukemia, lymphoma, glioma, breast, prostate, pancreas, bladder, melanoma and lung (page 6 of the Instant Action).

The Examiner indicated that Applicants' arguments of May 19, 2005, that neither Fogarty itself nor any reference cited in Fogarty recites treatment of cancer with Ginkgo biloba extracts or with isolated GKB, were not persuasive. The Examiner maintains that Fogarty does teach "anti-tumor activity of the extracts of Ginkgo biloba leaf itself in Table 2 on col 13." The Examiner also indicated that Applicants' arguments that "Fogarty fails to teach or suggest to use a Ginkgo extract containing GKB or GKB to combat cancer cells characterized by an over-expression of PBR are similar to those raised for the rejections over DE '868 and EP '951" and were not found to be persuasive.

B) 35 U.S.C. § 102(e)

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 102(e) that forms the basis for the rejection under this section. As pointed out by the Examiner on page 5:

> (e) The invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treated defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

C) Amended and cancelled claims

Applicants note that claims 1, 5, 7, 8, and 16-24 have been amended in the instant specification, and claims 27-28 are new. Claims 2, 3, 9-15 and 26 have been cancelled from the instant application, thus the rejection thereof under 35 U.S.C. § 112, first paragraph, has been obviated for these claims.

D) Claims 1-3, 5-9, 12, 13, 15-24 and 26 are not anticipated by US 6,316,690 under 35 U.S.C. § 102(e)

Applicants respectfully reiterate in full the arguments made in Applicants' May 19, 2005 reply. Applicants also respectfully submit that the present amendments to the method of claim 1, and therefore of dependent claims 5-8, 16-24, 27 and 28, further distinguish Applicants' method from Fogarty as Fogarty fails to teach or suggest to the practitioner to determine whether the levels of PBR in breast cancer cells are elevated and, upon finding elevated levels of PBR (*i.e.*, at least 3-fold greater than a normal cell), to administer an effective amount of a Ginkgo biloba extract containing GKB or of isolated GKB to treat the breast cancer.

E) Request for withdrawal of rejection of claims 1-3, 5-9, 12, 13, 15-24 and 26 under 35 U.S.C. § 102(e)

Applicants submit that, for reasons cited above and amendments presented herein, the anticipation rejection of claims 1, 5-8, 16-24 and new claims 27-28 under 35 U.S.C. § 102(e) over Fogarty has been obviated. Applicants respectfully request that said rejection be withdrawn.

4. Claim Rejections – 35 U.S.C. § 103(a)

A) Rejection of claims 1-3, 5-24, and 26 under 35 U.S.C. § 103(a)

On pages 7-8 of the instant Office action, the Examiner rejects claims 1-3, 5-24, and 26 under 35 U.S.C. § 103 as obvious over U.S. Patent No. 6,316,690 (Fogarty). Fogarty employs an artificial system in which transgenic larvae of the fruit fly *Drosophila melanogaster* genetically engineered to express a v-myb transgene are treated with uncharacterized extracts of "Chinese herbs" to delay tumor progression in said larvae.

The Examiner maintains that:

> "Fogerty teaches a transgenic Drosophila melanogaster as the model to predict the ability of a compound's effectiveness in the treatment of cancer. One of the [sic] An ingredient used by Fogerty is Ginkgo biloba extract. Based on this model taught by Fogerty combined with the art known anti-tumor activity of Gingko biloba extracts also taught by Fogerty, it would have been obvious to one of ordinary skill in the art to use Ginkgo extract to treat various forms of cancer, with a reasonable expectation of success."

The Examiner goes on to allege that Applicants arguments were not persuasive because:

> "instant claims are drawn to a method of combating cancer and not to a model system or to 'a method of interaction of Ginkgo extract containing GKB or isolated GKB with peripheral-type benzodiazepine receptor protein.' Fogarty does teach the anti-tumor activity of extracts from leaves of Ginkgo biloba based on the model and therefore, one of ordinary skill in the art would be motivated to use these extracts to any cancer with a reasonable expectation of success. Instant specification contains no data on the in vivo applicability of these extracts on various types of cancer as claimed."

B) 35 U.S.C. § 103(a)

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 103(a) appearing on page 7 of the instant Office Action that forms the basis for the rejection under this section:

> 35 U.S.C. § 103(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

C) Amended and cancelled claims

Applicants note that claims 1, 5, 7, 8, and 16-24 have been amended in the instant specification, and claims 27-28 are new. Claims 2-3, 9-15 and 25-26 have been cancelled from the instant application, thus the rejection thereof under 35 U.S.C. § 112, first paragraph, has been obviated for these claims.

D) Claims 1-3, 5-24 and 26 are not obvious over US 6,316,690 under 35 U.S.C. § 103(a)

Applicants respectfully reiterate in full the arguments made in Applicants' May 19, 2005 reply. Applicants respectfully submit that the Examiner has not made a prima facie case for obviousness. *In re Vaeck* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) states that there are

three basic criteria to be met to establish a prima facie case of obviousness: 1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings, 2) there must be a reasonable expectation of success and 3) the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Applicants respectfully submit that the present amendments to the method of claim 1, and therefore of dependent claims 5-8, 16-24, 27 and 28, further distinguish Applicants method from Fogarty. Fogarty fails to teach or suggest all of the claim limitations of amended claim 1 because Fogarty fails to teach or suggest to the practitioner to determine whether the levels of PBR in a breast cancer cell are elevated, and, upon finding elevated levels of PBR (*i.e.*, at least 3-fold greater than a normal cell), to administer an effective amount of a Ginkgo biloba extract containing GKB or of isolated GKB to treat the breast cancer.

E) Request for withdrawal of rejection of claims 1-3, 5-24 and 26 under 35 U.S.C. § 103(a)

As Fogarty fails to teach or suggest all of the claim limitations of the presently amended claims, Applicants respectfully request that the rejection of claims 1, 5-8, 16-24 and 27-28 under 35 U.S.C. § 103(a) over Fogarty be withdrawn.

In summary, Applicants respectfully submit that the amendments to independent claim 1 and dependent claims 5-8, and 16-24, cancellation of claims 2-4, 9-15 and 25-26, and the introduction of claims 27 and 28 fully address the Examiner's concerns as detailed in the Final Office Action dated August 8, 2005 as well as his concerns voiced in the October 26, 2005 teleconference. Applicants submit that neither the DE '868, EP '951 nor Fogarty references relied upon by the Examiner, taken either alone or in combination, teach or suggest to the skilled artisan to determine whether levels of PBR in a breast cancer cell are elevated and to select for treatment with either a Ginkgo biloba extract containing GKB or with GKB alone those breast cancers with elevated levels of PBR.

REQUEST FOR CONTINUED EXAMINATION

Applicants respectfully request withdrawal of the finality of the Office Action mailed August 5, 2005 pursuant to the Request for Continued Examination under 37 C.F.R. §1.114 filed concurrently herewith. Applicants submit that all conditions required for the reopening of the prosecution of the instant application have been met, to wit, 1). prosecution of the instant application, a non-provisional utility application with a filing date after June 8, 1995, is closed due to the finality of the August 5, 2005 Office Action; 2). the above amendments meet the reply requirements of 37 C.F.R. §1.111; and 3). the requisite fee has been paid pursuant to the concurrently filed authorization for payment thereof from Applicant's deposit account.

CONCLUSION

Applicants respectfully submit that all claims are in a condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to telephone Applicant(s) attorney at (508) 478-0144 to facilitate prosecution of this application.

Respectfully submitted,

Date:
12/16/05

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